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The impact of Silymarin on antioxidant capacity of serum and lipid peroxidation in patients with severe pre-eclampsia

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ABSTRACT

Preeclampsia is a pregnancy-specific disorder. In this study, the impact of Silymarin was investigated on antioxidant capacity of serum and lipid peroxidation in patients with severe pre-eclampsia. 60 patients whose pregnancy were ended because of severe preeclampsia were entered the study. Patients were randomly divided into two groups of 30 case and control groups. In addition to current treatments for preeclampsia, case groups were administered 70 mg of Silymarin, 3 and 24 hours after the termination of pregnancy. The control group received placebo at the same time. Antioxidant capacity of serum and lipid peroxidation was checked 60 hours after the termination of pregnancy in two groups. At the baseline, the two groups were not significantly different in terms of criteria such as age, BMI. Peroxidation of lipids in maternal serum 60 hours after the termination of pregnancy were not significantly different in the two case and control groups ($P > 0.05$). Antioxidant capacity in maternal serum were significantly different in the two case and control groups. Silymarin is an herbal remedy that in many cases has beneficial results. It seems that this drug can be used in severe pre-eclampsia. However, as the risk of severe pre-eclampsia can predict long-term cardiovascular complications for the mother, design of studies with long-term use of antioxidant in pregnant women with severe preeclampsia and its long-term follow-up is recommended.

Keywords: Preeclampsia, Silymarin, antioxidant capacity, lipid peroxidation

INTRODUCTION

Pre-eclampsia is a multifactorial disease and is a major cause of maternal and fetal morbidity and mortality. Preeclampsia is regarded as a sudden onset of hypertension and proteinuria or end-organ failure after 20 weeks of pregnancy in women who already had normal blood pressure. Clinical protests of preeclampsia may be appeared at any time since the second half of the pregnancy or the first few days after delivery. In cases of severe preeclampsia may cause mother to suffer from disorders such as pulmonary edema, cerebral hemorrhage, Convulsion, impaired hepatic and renal impairment and even death and cause complications in newborn such as preterm delivery, stillbirth, neonatal growth restriction and neonatal admission in intensive care center [1].

The plasma lipid peroxidation that can cause endothelial damage and placental vascularization in preeclampsia [3, 4]. Several studies have reported imbalance between the antioxidants and lipid peroxidation in preeclampsia. Silymarin is the extract of *Silybum marianum*. Silymarin is a Medicinal plant and is the extract of *Silybum marianum*. Silybum was considered as a sacred medicine in ancient times and has long record in treatment

and has traditionally been used as a medicinal plant. In the first century AD, a Roman biologist called Pliny has stated that milky juice of this plant is useful in order to induce the secretion of bile. In 1968, scientists separated the three specific molecules of this plant called Silibinin, Silydianin, Silydiannin, Silychristin that today, collectively are called Silymarin. The date of the therapeutic use of this plant dated back to 2000 years ago and they were named as a liver protective agent in ancient Greek sources [5, 6]. Nowadays in several studies, the impact of Silymarin on different liver disorders and complications has been examined, which in most cases have a significant beneficial effects no remarkable side effects has been mentioned. In this study, the impact of Silymarin that is an herbal drug with antioxidant properties was investigated upon the effects of severe preeclampsia. In this study, the impact of Silymarin on different symptoms of severe preeclampsia was investigated in pregnant women whose pregnancies have been terminated because of severe preeclampsia.

MATERIALS AND METHODS

The study was a double-blind clinical trial intervention with Ict code: 201509042388/N1 and the study population was selected among the patients hospitalized in Hajar hospital of Shahrekord that their pregnancy was terminated because of severe preeclampsia. This study was carried out between April 2014 and September 2015. Considering inclusion criteria, the patients who were eligible for the study were selected and full description of pre-eclampsia and the type of study have been given to them. A total of 60 people who had consent to enter the study and signed a consent form were enrolled.

Inclusion criteria were:

1. The mother's age was between 20 and 30 years.
2. BMI of mothers was between 20 and 24 are.
3. When gestational age was between 35 and 42 weeks.
4. The patient's blood pressure before pregnancy termination was greater than 140/90 mm Hg.
5. The presence of proteinuria in random urine sample before pregnancy termination
6. Absence of history of hypertension, diabetes, kidney disease, collagen vascular disease and other cardiovascular diseases
7. Nulliparous mothers and abortion or no previous pregnancy.
8. No smoking or alcohol consumption history in mother
9. Singleton not molar pregnancies.
10. Termination of pregnancy is indicated for patients with severe preeclampsia.
11. Patient satisfaction in participating in the study and the consent form is signed.
- 12-Lack of preeclampsia before inclusion in the study

Exclusion criteria were as follows:

1. The lack of consent to participate in the study
2. Sufferance of the patient from eclampsia

After examination of inclusion criteria, 60 patients entered the study and were divided into two case and control groups. The patients were assigned into two groups was based on randomness, the priority of reference. Besides, it was attempted that the patients in both groups were matched for age and initial lab results.

Having entered patients to study, their basic information was recorded in their related form. The patient's age is calculated based on his year of birth and was recorded in his form. Patient weight was measured using a weigh scale analog and was recorded based on kg in the form of each patient. Patient's height and BMI was measured by a tape meter based on meter (M) and BMI was measured based on kilograms per square meter (kg/m^2). The patient's type of delivery (vaginal delivery or cesarean) extracted from the patients files and was recorded in the related form of each patient. Birth weight of babies was measured using an infant measuring device and was recorded in the related form of each patient.

In the baseline, survey results for each patient was extracted from their file and was recorded in in both case and control groups, patients received routine severe pre-eclampsia treatments.

60 hours after receiving the first dose of drug, serum antioxidant capacity was measured using the Randox kit, Uk and by auto analyzer COBAS-MIRA (manufactured by Roche) and the results is registered based on mmol/L in the form of each patient.

60 hours after receiving the first dose of lipid peroxidation, serum in patients was measured with thiobarbituric acid reaction with Malondialdehyde serum with the help of fluorescence device and the results were recorded based on a mmol/L in the related form of each patient. The measurement procedure was as follows: After adding 50 microliters of serum samples in one ml of distilled water, 1 ml of thiobarbituric acid (2 mmol per liter) was added to acetic acid (8.75 mmol per liter). The samples were heated for 60 minutes at a temperature of 95 ° C and then 25 µl of chloridric acid solution (5 mmol per liter) was added. Finally, after adding 3.5 ml of 1-butanol to the sample and making them centrifuged (at 3000 rpm for 10 minutes), the absorbing layer of butanol in the excitation wavelength and emission wavelength is read 525 nm and 547 nm by fluorometry device (NONTRON SFM 25 A, Italy). Furthermore, patients were also evaluated for the occurrence of Convulsion (eclampsia) and hospital stay and the results have been recorded in their related forms. At the end, the two groups were compared in terms of age, BMI, birth weight, gestational age within termination of pregnancy, serum antioxidant capacity, lipid peroxidation level. The data were analyzed through SPSS software.

RESULTS

This study was performed to evaluate the effect of Silymarin on antioxidant capacity of serum and lipid peroxidation in patients with severe pre-eclampsia in Hajar hospital of Shahrekord. The following results have been achieved. In this study, two groups of 30 women with severe preeclampsia that they had been involved in the termination of pregnancy were participated.

The mean values of antioxidant capacity in maternal serum, 60 hours after the termination of pregnancy was 1.4 ± 0.23 in the intervention group and 0.9 ± 0.18 in the controls group that the difference between the two groups was statistically significant ($P > 0.05$). Peroxidation of lipids in maternal serum 60 hours after the termination of pregnancy in the intervention group was 0.88 ± 0.17 and 0.86 ± 0.11 in the control group that there is no significant difference between the two groups ($P > 0.05$).

This means that the two groups at baseline had relatively equal conditions that reduced the impact of confounding factors in the analysis of collected data during the study. In the case group treated with Silymarin, serum antioxidant capacity of mothers compared to that of control group that was significantly higher that this finding correspond with antioxidant properties of Silymarin. Thus, it seems that these parameters have not been affected by the intervention (treatment with Silymarin) and it appears that further studies are needed to approve or reject the effect or lack of effect of antioxidant factors in this study. There was no significant difference between the two groups regarding to Other parameters measured during the study. Since severe pre-eclampsia is one of the concerns in obstetric medicine and since nowadays, Silymarin is regarded as one of the safe treatment having antioxidant properties, it seems that further studies with higher doses of Silymarin to evaluate its effect on treatment of severe pre-eclampsia would be beneficial and may present an effective antioxidant treatment for these patients. As Silymarin nowadays is used as an adjuvant treatment (in the research stage) to help to treat the jaundice [8], it seems as if it is proved to be safe, several studies with higher doses of Silymarin for mother can be administered (no worries about the effects of the drug in breast milk) in order that the effects of this drug is examined in detailed in treatment of severe pre-eclampsia. As the risk of severe pre-eclampsia can predict long-term cardiovascular complications for the mother, design of studies with long-term use of antioxidant in pregnant women with severe preeclampsia and its long-term follow-up is recommended.

DISCUSSION

At present, there is limited number of treatments for preeclampsia and several studies have investigated the effect of antioxidants in the prevention and treatment of preeclampsia. The aim of this study was to evaluate the effect of Silymarin on antioxidant capacity of serum and lipid peroxidation in patients with severe pre-eclampsia. In this study, the antioxidant effect of silymarin was investigated which is theoretically impede the creation and probably the restoration of endothelial lesions in liver disorders and platelet mother in severe preeclampsia

In a study in Ireland, the impact of silymarin on inflammatory cytokines produced by mononuclear cells was investigated in preeclampsia. In this study, it was observed that silymarin caused to decrease the secretion of tumor necrosis factor alpha and interleukin-1 beta by PBMC in patients with pre-eclampsia and it seems that silymarin exerts its antioxidant effects through these inflammatory mediators[9].

In comparing the results of this study that was to evaluate the performance of silymarin at the cellular level with our study, it was observed that in both studies, silymarin demonstrated its antioxidant effects in preeclampsia, but in this study, the impact of silymarin on the cellular level with biochemical approaches have been studied, while in our study, clinical approach to preeclampsia is considered.

In a study in the Netherlands, the effect of combination therapy of vitamin E and C in the prevention of preeclampsia has been investigated and it was observed that the prescription of above-mentioned vitamins is significantly effective in the prevention of preeclampsia [10].

Given to the fact that silymarin has antioxidant properties similar to these vitamins, it seems that if safety of silymarin in the pregnancy is confirmed, it may be designed some studies to evaluate the effect of silymarin on prevention of pre-eclampsia.

In a study in Shiraz, the effect of adding silymarin to the renin-angiotensin inhibitors in reducing proteinuria in type II diabetes is discussed. In this study carrying upon patients with type II diabetes and diabetic nephropathy, in the case group, in addition to inhibitors of the renin-angiotensin, patients had received 2 tablet of Silymarin 140 mg daily for three months that at the end, proteinuria was significantly decreased in the case group and the amount of lipid peroxidation was significantly lower[11]. in the case group,

In comparing the results of this research with our study, we observed that in our study, silymarin has no effect on reducing proteinuria while in the above-mentioned study, Silymarin reduces proteinuria in patients with diabetic nephropathy.

The reason for this difference could be due to differences in the dose of silymarin in the study. However, in the above-mentioned study, Silymarin reduced lipid peroxidation that this was not happened in our study and its reason may be due to differences in the nature of the illness or the dose and duration of consumption of Silymarin.

Besides, in the intervention group that was treated with Silymarin, serum antioxidant capacity of mother was significantly higher than that of control group that this finding corresponds with antioxidant properties of Silymarin.

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